

assembly of the viral coat (e.g., by suppressing cleavage of the precursor coat protein). gp120 is a component of the viral coat. It is produced by a cell under protease inhibition therapy, and can be detected immunologically, but it is not efficiently assembled into active viral coat, and infectious virus is not produced.

Furthermore, Chun et al, *Nature*, 387:183-188, 1997, identify unintegrated, replication defective HIV as the most prevalent form of HIV DNA in resting and activated CD4 cells. See, e.g., Chun et al., Page 183, Abstract; Page 187, 1st column, third paragraph. Although this form of HIV can presumably be detected using nucleic acid based tests, it is certainly not an indicator of infectious virus. To the contrary, such virus can not replicate in the cell. Again, this shows the dissociation of the expression of HIV antigens (e.g., nucleic acids, polypeptides, etc.) from the ability of the HIV to replicate itself and produce infectious particles.

Fessel et al., *J. Acq. Imm. Def. Synd.*, 23:314-320, 2000 (attached), similarly show that "indexes of HIV infection" can not interchangeably be used to diagnose productive infection, and hence, underlying latent viral load. According to this paper, "The PR [partial responders] and CF [complete failures] both had high plasma HIV RNA levels but only a small fraction of this HIV represented HIV particles that were capable of replicating in tissue culture." Fessel et al., Page 317, Column 1, line 8. In other words, the presence of HIV RNA in the plasma, although clear evidence of HIV infection, does not mean that such RNA is actually biologically-active and infectious. Additionally, as shown in Table 1, both PR and CR have comparable levels of HIV DNA copies in PBMCs (e.g., 4.243 v. 4.634), but significant differences (20-fold) in the number of infectious particles detected (e.g., 42 v. 2.165).

In summary, the rejection is based on the unsupported assumption that detection of gp120 would have been expected to be a measure of latent viral load. As discussed above, there is no simply no evidence of record to support this allegation.

In view of these comments, withdrawal of the rejection is respectfully requested.

Respectfully submitted,

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